U.S. FOOD & DRUG ADMINISTRATION

Public Workshop: New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products (OINDPs)

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GDUFA Regulatory Science Initiatives for Generic Orally Inhaled and Nasal Drug Products (OINDPs)

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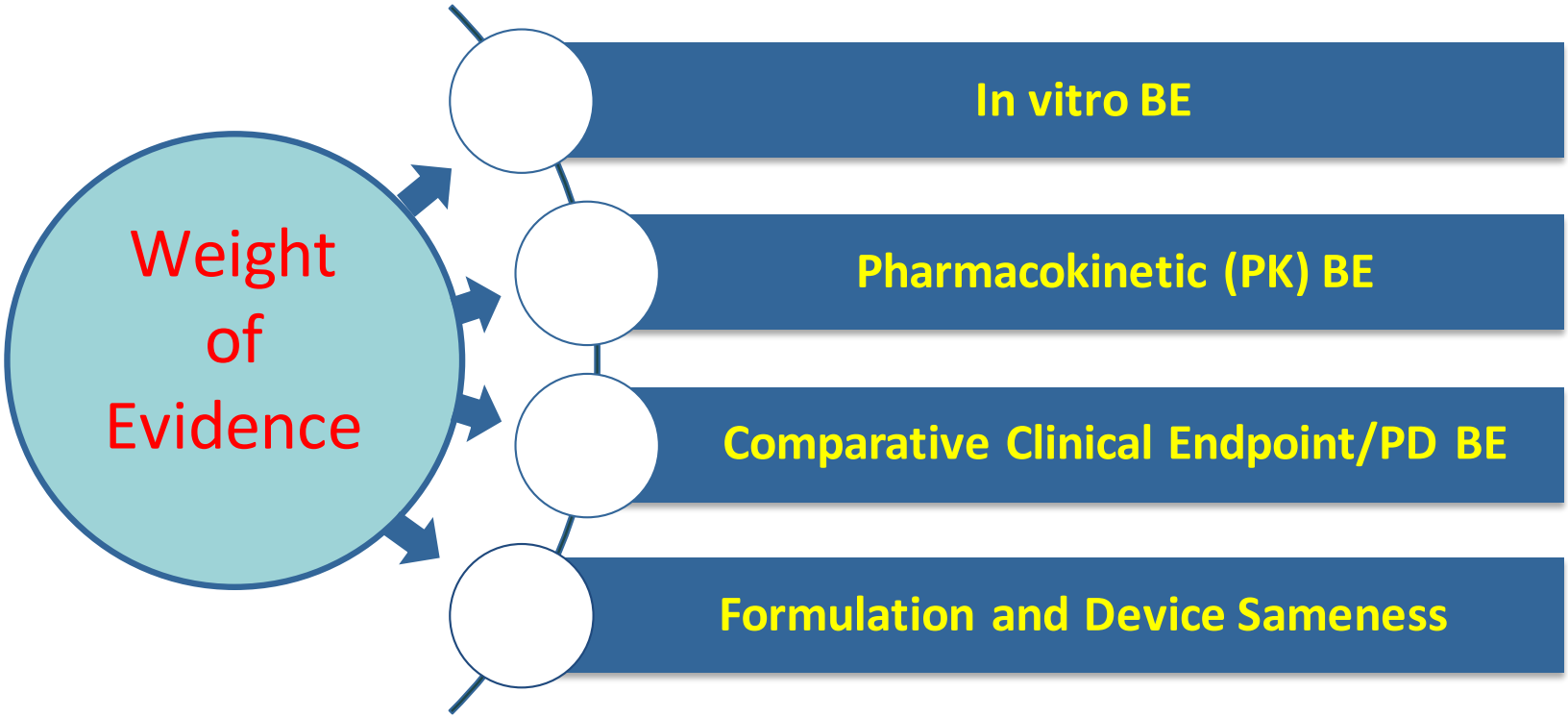
Challenges with Demonstration of TE of Locally Acting Generic OINDPs

- Drug delivery is local to the site of action (e.g., lung tissue), not systemic
  - Intended target effect does not rely primarily on systemic absorption
  - Challenges to measuring local effect
- Device is integral part of the delivered dose
- Several factors influencing drug local and systemic bioavailability include:
  - Patient-device interactions
  - Device-formulation interactions
  - Regional drug distribution
  - Local dissolution/permeability/clearance

TE: therapeutic equivalent

Weight of Evidence BE Approach



- Currently recommended for locally acting nasal suspensions, dry powder inhalers (DPIs) and metered dose inhalers (MDIs) **(accounts for 60% of OINDPs)**
- Comparative clinical endpoint studies are long and costly, and least sensitive to formulation differences

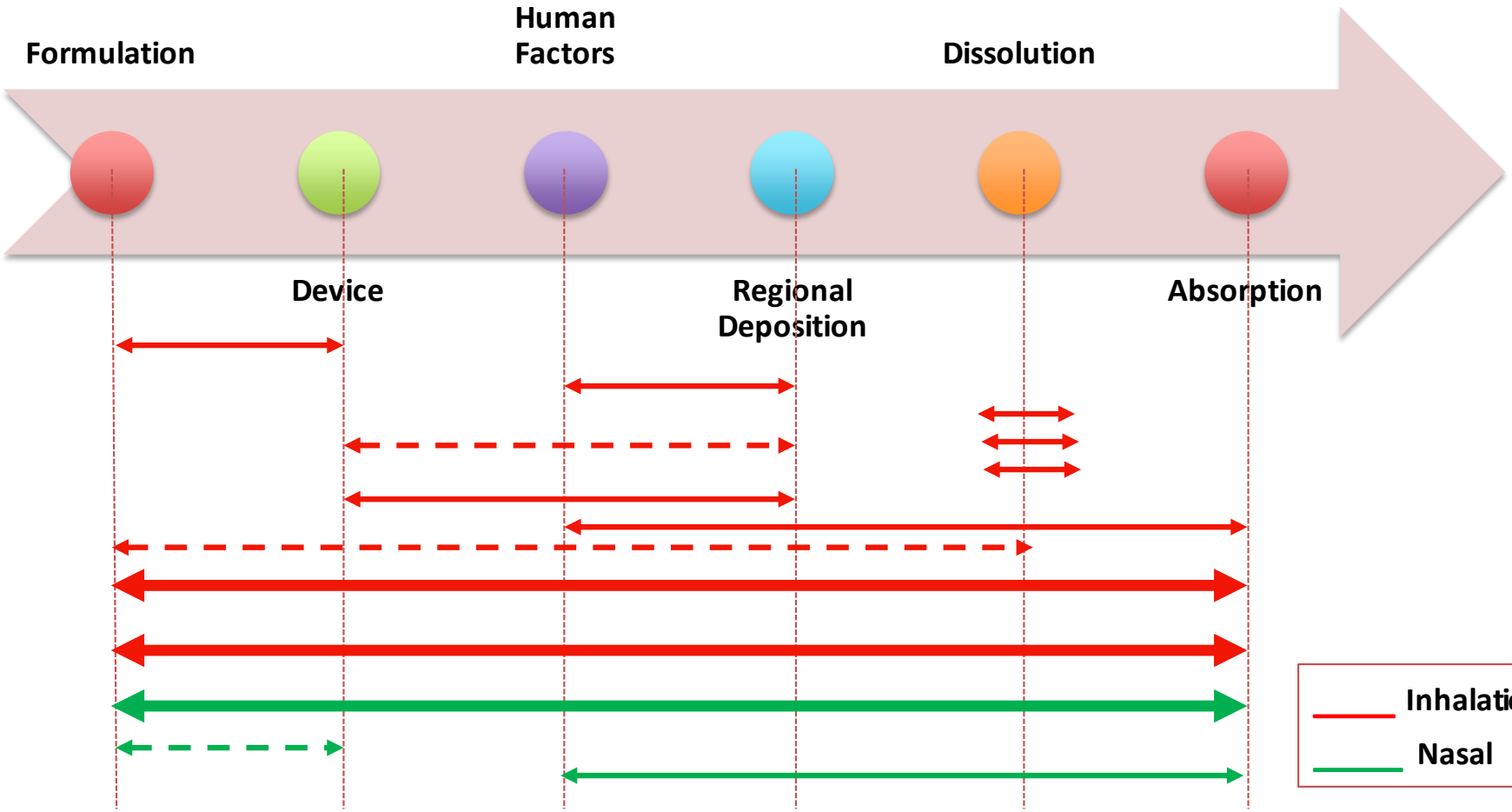
GDUFA Regulatory Science Initiative for OINDPs

- Identification of formulation and device variables which are important for successful development of generic OIDPs

- Development of clinically relevant in vitro and in silico tools and methodologies for prediction of in vivo regional drug deposition and dissolution from OINDPs, and to assess their applicability in generic OINDPs development programs

- Identification, validation and standardization of novel techniques that may have the potential to reduce the burden of current BE requirements for generic OINDPs.

Scope of GDUFA Regulatory Science Initiative for OINDPs



Research Projects: Completed or Close to Completion

Formulation

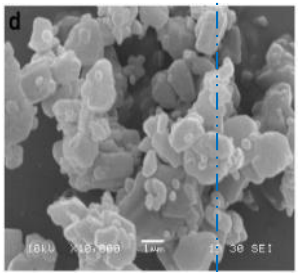
Device

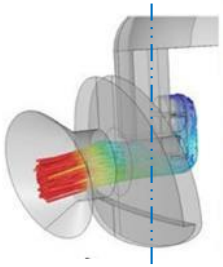
Human Factors

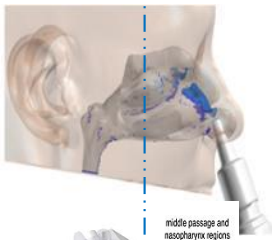
Regional Deposition

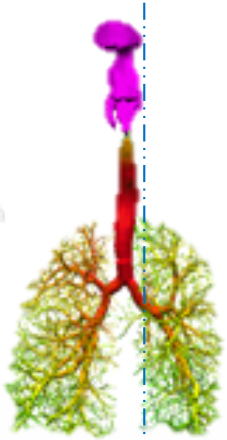
Dissolution

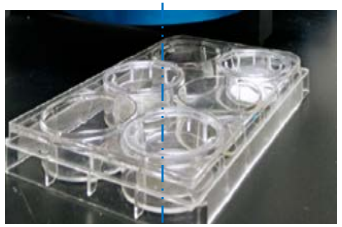
Absorption

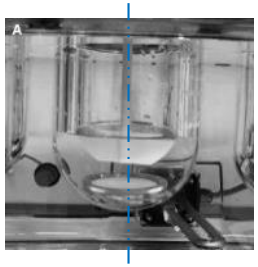


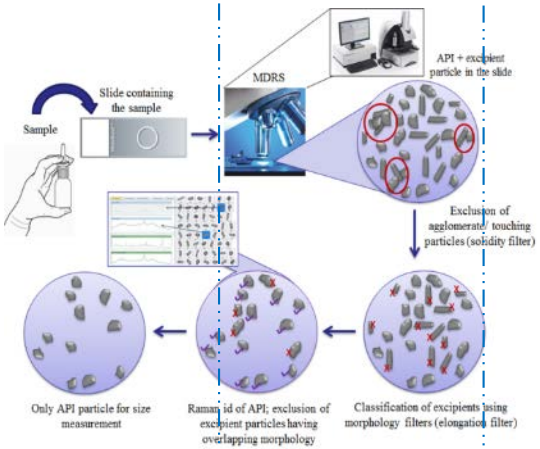


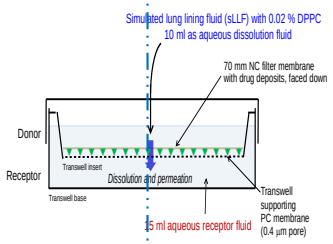












New Research Projects in FY 17

- Investigating the Microstructure of Dry Powder Inhalers using Orthogonal Analytical Approaches (University of Bath)

- Investigating Orthogonal Analytical Approaches to Demonstrate Bioequivalence of Nasal Suspension Formulations (University of Bath)

- Patient's Perception of Dry Powder Inhaler Airflow Resistance (Imperial College of London)

2018 Research Priorities for OINDPs

- Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery
- Develop more efficient alternatives to the use of forced expiratory volume in one second (FEV1) clinical endpoint BE studies for inhaled corticosteroids
- Develop alternatives to clinical endpoint BE studies for locally-acting nasal products
- Evaluate the impact of identified differences in the user-interface on the substitutability of generic drug-device combination products

GDUFA Regulatory Science Priorities for Fiscal Year 2018;
https://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/UCM582777.pdf

Impact of Regulatory Science Initiative

- Provided insight into many manufacturing processes and critical parameters that influence performance of complex OINDPs from a BE perspective.
- Informed the development of 39 PSGs for OINDPs, which provides a roadmap toward ANDA approval for this complex class of product.
- Boosted development of next generation tools for faster and more cost-effective BE assessment of OINDPs in future.

Getting Feedback on Innovative BE Approaches

- GDUFA II Pre-ANDA product development meetings for complex products allows FDA to engage with industry to support innovative and efficient methods to demonstrate equivalence
  - new development strategies when no PSG is available
  - development of alternative development (i.e., change in study type, such as in vitro to clinical) for a complex product for which FDA has issued a product-specific guidance
- The pre-ANDA program is designed to accelerate access to generic versions of complex products, including OINDPs.
- A complete meeting package containing clear and specific questions that are supported by appropriate data.

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM578366.pdf

For More Information

- https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm

Today's Workshop

1. Predictive Dissolution Methods for OINDPs
2. Novel Analytical Tools for Characterization of Nasal Suspensions
3. Realistic Models for Prediction of Regional Drug Deposition from OINDPs
4. Computational Models to Understand In Vivo Performance of OINDPs